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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,894	12/15/1999	MARC PIECHACZYK	19141-007	5731

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	35

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/341,894	PIECHACZYK ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,35-40,42 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,35-40,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *August 8, 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on December 11, 2003, paper number 33, has been entered.

DETAILED ACTION

This application is a 371 national stage filing of PCT/FR98/00081, filed January 16, 1998 which claims benefit to foreign application FR 97/00540, filed January 20, 1997 in France.

As requested in Applicants' request for continued examination the amendment filed May 29, 2003, paper number 31(indicated as mailed May 29, 2003 by Applicants) has been entered. Claims 1-31, 33-34 and 41 have been canceled. Claim 43 has been added.

Claims 32, 35-40, 42 and 43 are pending and currently under examination.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 35-40, 42 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The amendment to the claims to delete the portions of the claim considered new matter has obviated the basis of the rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 35-40, 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 32, 40 and 42 are vague and unclear in the recitation of "wherein the nucleotide sequence encoding the antibody is not modified" because the extent of what can or can not be modified is not clearly set forth. For example, dependent claims set forth that the antibody produced is a fragment (see claim new claim 43), where this would clearly indicate that a coding sequence has been modified to be shorter than usual. Further, any sequence taken out of its context in the genome could be considered modified, however the instant claims clearly require that the use of vectors and heterologous promoters. Moreover, the language of the claim recites 'comprising' which allows for the antibody sequence to contain other sequences (for example consensus sequences that allow the protein to be secreted). It is unclear if the claims encompass any antibody coding sequence in any context, as long as the specific coding sequence isolated

from nature is not affected, thus would not encompass sequences which are modified but still encode the same protein. Finally, the claims are unclear because they now require that the antibody be secreted in a particular context, however the sequences encompass providing expression of portions of an antibody that clearly would not be secreted. While the claim encompass sequences that are not modified, the metes and bounds are unclear to what extent this negative limitation encompasses because the claims clearly require modifications for expression and secretion. Dependent claims are included in the basis of the rejection because they fail to clarify the basis of the rejection only indicating how the sequence is modified relative to its chromosomal location and context in the genome.

In addition, the metes and bounds encompassed by 'therapeutic' are vague and unclear. Initially, it is not clear to whether it is the cell that is therapeutic or the antibody produced by the expression vector is therapeutic. If it is the cell, it is unclear how or what type of therapeutic affect the cell itself is supposed to encompass. If it is directed to the antibody produced, the ability of an antibody to be therapeutic depends on many factors beyond the context of the claim relying on specific amounts of expression, circulation, and half life in circulation, and also would be dependent on the context of use. For example, while an antibody delivered directly to a tumor may be cytotoxic to the tumor cells and be considered to have therapeutic affect, there is not nexus between this and the expression of the same antibody at some other location having the same affect. Moreover, the amount of affect that one would consider 'therapeutic' is not specifically set forth in the specification nor the claims, therefore the ability to adequately access an antibody to therapeutic would only relevant to an individual and be subject to change from one individual to another.

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32, 35-40, 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright *et al.*

Applicants note the amendments to the claims and the requirements of a reference for anticipation citing *Scripps clinic & Research Foundation v. Genentech Inc.* Applicants argue that Wright *et al.* does not anticipate the claims because it provides teachings for the *in vitro* production of monoclonal antibodies and that the non-lymphoid cells taught are transformed cell lines which would not be suitable for implantation and would not be maintained in a mammal for several months. See Applicants' amendment, pages 5-6. Applicants' arguments have been fully considered but not found persuasive.

In the instant case, any cell depending on its use or means of delivery would meet the limitation of intended use of this embodiment because the appropriate conditions would be found to maintain the cells. Furthermore, transformed cells are capable of proliferating in the form of a tumor in animal models, thus the cells of Wright *et al.* would be maintained in mammal. There is no guidance on the 'suitability' of any particular cell type which is encompassed by the instant claims and again would be dependent on an intended use. Further, it is noted that the

transformed cell lines taught by Wright *et al.* are similar to those disclosed in the working examples in the instant specification. Wright *et al.* disclose non-plasmacyte cells which contain heterologous polynucleotide sequences which express and secrete an antibody (summarized in abstract). Wright *et al.* discuss the use of the antibodies for therapeutic purposes clearly indicating that the antibody can be therapeutic (page 125). Finally, Wright *et al.* give guidance and provide specific methods for the use of a variety of vectors and expression systems for expressing antibodies in cells which react to both viral and cancer antigens. Therefore, Wright *et al.* anticipates the claims.

Claims 32, 35-40, 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevenson *et al.*

Applicants note the amendments to the claims and the requirements of a reference for anticipation citing *Sripps clinic & Research Foundation v. Genentech Inc.* Applicants argue that Stevenson *et al.* does not anticipate the claims because it teaches modified coding sequence for antibodies not entire unmodified antibody as required by the pending claims, in particular claims 32 and 40. See Applicants' amendment, pages 6-7. Applicants' arguments have been fully considered but not found persuasive.

Applicants' arguments that the claims encompass only using the entire coding sequence of an antibody are noted, however the claims do not recite this, and as set forth in the rejection made under 35 USC 112, second paragraph, do appear to require solely this limitation. One reasonable interpretation encompassed by the metes and bounds of the claims would be in light of the teachings of the specification is that the polynucleotide sequences encoding any fragment

of an antibody has not been modified. Stevenson *et al.* teach mammalian expression vectors capable of providing the expression and production of various antibodies which are secreted from the cells (see figure 1). With regard to the expression of ScFv fragments, it is noted that Stevenson *et al.* does not alter the sequences that encode portions of the antibody, leaving the native V_H and V_L regions unmodified. The antibody produced by Stevenson *et al.* therefore represents a native unmodified antibody molecule. The antigen to which the antibody reacts is directed to a tumor related epitopes (page 213). Further, the V_H1 portion of the sequence contains the leader sequence allowing for the exit of the protein from the cell (see figure 2 and legend). Since a reasonable interpretation of the claims includes native unmodified fragments of an antibody, the vectors and cells transduced with said vectors which express an antibody as taught by Stevenson *et al.* anticipates the claims.

Claims 32, 35-40, 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen *et al.* (1994).

Claims 32, 35-40, 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen *et al.* (1996).

Applicants traverse the teaching of the two Chen *et al.* references together. Applicants argue that Chen *et al.* does not anticipate the claims because it teaches modified antibodies not a native unmodified antibody as required by the pending claims, and the cells used by Chen *et al.* would not be considered for therapeutic use. See Applicants' amendment, page 7. Applicants' arguments have been fully considered but not found persuasive.

As noted above, a reasonable interpretation of an embodiment within the metes and bounds of the claims in light of the teachings of the specification is that the polynucleotide sequences encoding the antibody has not been modified. Chen *et al.* teach mammalian expression vectors capable of providing the expression and production of various antibodies which are secreted from the cells (page 5932, figure 1). With regard to the expression of Fab fragments, it is noted that Chen *et al.* does not alter the sequences that encode portions of the antibody, leaving the native V_H, C_H, C_K and V_K regions unmodified. The antibody produced by Chen *et al.* therefore represents a native unmodified antibody molecule. The antigen to which the antibody reacts is directed to a the gp120 molecule of HIV (abstract, page 5932). Further, Chen et al. teach signal leader sequences allowing for the exit of the protein from the cell (see figure 1). Similarly, the second reference of Chen *et al.* teach mammalian expression vectors capable of providing the expression and production of various antibodies which are secreted from the cells (page 1517, figure 1). With regard to the expression of Fab fragments, it is noted that Chen *et al.* does not alter the sequences that encode portions of the antibody, leaving the native V_H, C_H, C_L and V_L regions unmodified. The antibody produced by Chen *et al.* therefore represents a native unmodified antibody molecule. The antigen to which the antibody reacts is directed to a the gp120 molecule of HIV (abstract, page 1515). Further, Chen *et al.* teach signal leader sequences allowing for the exit of the protein from the cell (see figure 1). Since a reasonable interpretation of a native unmodified molecule includes native unmodified fragments of an antibody, the vectors and cells transduced with said vectors which express an antibody as taught by Chen *et al.* anticipates the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

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